Risperidone versus other atypical antipsychotics for schizophrenia.

Abstract:
In many countries of the industrialised world second-generation ("atypical") antipsychotics (SGAs) have become the first line drug treatment for people with schizophrenia. The question as to whether and if so how much the effects of the various SGAs differ is a matter of debate. In this review we examined how the efficacy and tolerability of risperidone differs from that of other SGAs. To evaluate the effects of risperidone compared with other atypical antipsychotics for people with schizophrenia and schizophrenia-like psychosis.

Electronic searching We searched the Cochrane Schizophrenia Group Trials Register (April 2007) which is based on regular searches of BIOSIS, CENTRAL, CINAHL, EMBASE, MEDLINE and PsycINFO.
Reference searching We inspected the references of all identified studies for more trials.
Personal contact We contacted the first author of each included study for missing information.
Drug companies We contacted the manufacturers of all atypical antipsychotics included for additional data. We included all randomised, blinded trials comparing oral risperidone with oral forms of amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, sertindole, ziprasidone or zotepine in people with schizophrenia or schizophrenia-like psychosis. We extracted data independently. For dichotomous data we calculated risk ratio (RR) and their 95% confidence intervals (CI) on an intention-to-treat basis based on a
random-effects model. We calculated numbers needed to treat/harm (NNT/NNH) where appropriate. For continuous data, we calculated mean differences (MD), again based on a random-effects model. The review currently includes 45 blinded RCTs with 7760 participants. The number of RCTs available for each comparison varied: four studies compared risperidone with amisulpride, two with aripiprazole, 11 with clozapine, 23 with olanzapine, eleven with quetiapine, two with sertindole, three with ziprasidone and none with zotepine. Attrition from these studies was high (46.9%), leaving the interpretation of results problematic. Furthermore, 60% were industry sponsored, which can be a source of bias. There were few significant differences in overall acceptability of treatment as measured by leaving the studies early. Risperidone was slightly less acceptable than olanzapine, and slightly more acceptable than ziprasidone in this regard. Risperidone improved the general mental state (PANSS total score) slightly less than olanzapine (15 RCTs, n = 2390, MD 1.94 CI 0.58 to 3.31), but slightly more than quetiapine (9 RCTs, n = 1953, MD -3.09 CI -5.16 to -1.01) and ziprasidone (3 RCTs, n = 1016, MD -3.91 CI -7.55 to -0.27). The comparisons with the other SGA drugs were equivocal. Risperidone was also less efficacious than olanzapine and clozapine in terms of leaving the studies early due to inefficacy, but more efficacious than ziprasidone in the same outcome. Risperidone produced somewhat more extrapyramidal side effects than a number of other SGAs (use of antiparkinson medication versus clozapine 6 RCTs, n = 304, RR 2.57 CI 1.47 to 4.48, NNH 6 CI 33 to 3; versus olanzapine 13 RCTs, n = 2599, RR 1.28 CI 1.06 to 1.55, NNH 17 CI 9 to 100; versus quetiapine 6 RCTs, n = 1715, RR 1.98 CI 1.16 to 3.39, NNH 20 CI 10 to 100; versus ziprasidone 2 RCTs, n = 822, RR 1.42 CI 1.03 to 1.96, NNH not estimable; parkinsonism versus sertindole 1 RCT, n = 321, RR 4.11 CI 1.44 to 11.73, NNH 14 CI 100 to 8). Risperidone also increased prolactin levels clearly more than all comparators, except for amisulpride and sertindole for which no data were available. Other adverse events were less consistently reported, but risperidone may well produce more weight gain and/or associated metabolic problems than amisulpride (weight gain: 3 RCTs, n = 585, MD 0.99 CI 0.37 to 1.61), aripiprazole (cholesterol increase: 1 RCT, n = 83, MD 22.30 CI 4.91 to 39.69) and ziprasidone (cholesterol increase 2 RCTs, n = 767, MD 8.58 CI 1.11 to 16.04) but less than clozapine (weight gain 3 RCTs n = 373, MD -3.30 CI -5.65 to -0.95), olanzapine (weight gain 13 RCTs, n = 2116, MD -2.61 CI -3.74 to -1.48), quetiapine (cholesterol increase: 5 RCTs, n = 1433, MD -8.49 CI -12. 23 to -4.75) and sertindole (weight gain: 2 RCTs, n = 328, MD -0.99 CI -1.86 to -0.12). It may be less sedating than clozapine and quetiapine, lengthen the QTc interval less than sertindole (QTc change: 2 RCTs, n = 495, MD -18.60 CI -22.37 to 14.83), produce fewer seizures than clozapine (2 RCTs, n = 354, RR 0.22 CI 0.07 to 0.70, NNT 14 CI 8 to 33) and less sexual dysfunction in men than sertindole (2 RCTs, n = 437, RR 0.34 CI 0.16 to 0.76, NNT 13 CI 8 to 33). Risperidone seems to produce somewhat more extrapyramidal side effects and clearly more prolactin increase than most other SGAs. It may also differ from other compounds in efficacy and in the occurrence of other adverse effects such as weight gain, metabolic problems, cardiac effects, sedation and seizures. Nevertheless, the large proportion of participants leaving studies early and incomplete reporting of outcomes makes it difficult to draw firm conclusions. Further large trials, especially comparing risperidone with those other new drugs for which only a few RCTs are available, are needed.